L Number	Hits	Search Text	DB	Time stamp
1	17718	retrovir$15	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/03/08 14:04
7	7505	retrovir$15 and (MULV or MLV or moMLV or murine or moloney)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/03/08 14:05
13	5407	(retrovir$15 and (MULV or MLV or moMLV or murine or moloney)) and (U3 or rre or rev or tat or LTR)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/03/08 14:06
19	2553	((retrovir$15 and (MULV or MLV or moMLV or murine or moloney)) and (U3 or rre or rev or tat or LTR)) and (donor or acceptor)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/03/08 14:06
25	1241	(((retrovir$15 and (MULV or MLV or moMLV or murine or moloney)) and (U3 or rre or rev or tat or LTR)) and (donor or acceptor)) and HIV	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/03/08 14:07
37	11722	("435/320.1").CCLS.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/03/08 14:08
43	421	(("435/320.1").CCLS.) and ((((retrovir$15 and (MULV or MLV or moMLV or murine or moloney)) and (U3 or rre or rev or tat or LTR)) and (donor or acceptor)) and HIV)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/03/08 14:08
49	35	((("435/320.1").CCLS.) and ((((retrovir$15 and (MULV or MLV or moMLV or murine or moloney)) and (U3 or rre or rev or tat or LTR)) and (donor or acceptor)) and HIV)) and (HIV SAME U3)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/03/08 14:11
55	26	((("435/320.1").CCLS.) and ((((retrovir$15 and (MULV or MLV or moMLV or murine or moloney)) and (U3 or rre or rev or tat or LTR)) and (donor or acceptor)) and HIV)) and (HIV SAME U3 SAME LTR)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/03/08 14:11
-	27	KINGSMAN-ALAN-JOHN	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/03/08 14:04
-	20	KINGSMAN-ALAN-JOHN and retrovir$15	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/03/07 10:25
-	17718	retrovir$15	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/03/07 10:28
-	90	retrovir$15 and (HIV WITH U3)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/03/07 10:29
-	58	retrovir$15 and (HIV WITH U3 WITH R)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/03/07 10:29
-	34	(retrovir$15 and (HIV WITH U3 WITH R)) and REV	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/03/07 11:24
-	1	LISZIEWCZ-JULIANNA	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/03/07 11:25
-	2	LISZIEWCZ-J$15	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/03/07 11:25

(FILE 'HOME' ENTERED AT 12:49:22 ON 08 MAR 2002)

FILE 'MEDLINE, AGRICOLA, CANCERLIT, SCISEARCH, CAPLUS, BIOSIS, MEDICONF'
ENTERED AT 12:49:31 ON 08 MAR 2002

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L1         22379 S RETROVIR? VECTOR?
L2          1081 S L1 AND (MULV OR MLV )
L3          1082 S L1 AND (MULV OR MLV OR MOLV)
L4           189 S L1 (L) 5(W)LTR
L5            55 S L4 AND (U3 OR RRE OR REV OR TAT)
L6            21 DUP REM L5 (34 DUPLICATES REMOVED)
L7            21 SORT L6 PY
L8          7387 S L1 AND (MULV OR MLV OR MOMLV OR MURINE OR  MOLONEY)
L9            12 S L8 AND (HIV (S) 5-LTR)
L10            5 DUP REM L9 (7 DUPLICATES REMOVED)
L11            5 SORT L10 PY
L12          659 S L8 AND HIV
L13          224 S L12 AND (U3 OR RRE OR REV OR TAT)
L14           91 DUP REM L13 (133 DUPLICATES REMOVED)
L15           46 S L14 AND PY<=1997
L16           46 SORT L15 PY
L17           15 S L2 AND (SPLICE AND DONOR OR ACCEPTOR)
L18           10 DUP REM L17 (5 DUPLICATES REMOVED)
L19           10 SORT L18 PY
L20            3 S L14 AND HIV (S) 5-LTR

=> d an ti so au ab pi l20 3

L20  ANSWER 3 OF 3  CAPLUS  COPYRIGHT 2002 ACS
AN   1998:268634  CAPLUS
DN   128:304785
TI   Construction and characterization of HIV and other lentiviral
     vectors
SO   PCT Int. Appl., 31 pp.
     CODEN: PIXXD2
IN   Kingsman, Alan John; Kingsman, Susan Mary
AB   Retroviral vector particles capable of infecting and
     transducing non-dividing mammalian target cells, which vector particles
     may be based on lentiviruses such as HIV and which have an RNA
     genome constructed so as to provide in the DNA provirus a non-lentiviral
     expression control element in the 5'LTR of the
     provirus.  These vectors, designated LLD (for lentiviral LTR-deleted) can
     be used to infect and transduce mammalian cells.  The method is
     exemplified by use of the U3 and promoter regions of
     murine leukemia virus in construction of LLD vectors.
     PATENT NO.        KIND  DATE          APPLICATION NO.  DATE
     ----------------  ----  --------      ---------------  --------
PI   WO 9817816         A1   19980430      WO 1997-GB2858   19971017
         W:  AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
             DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR,
             KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ,
             PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG,
             US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR,
             GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA,
             GN, ML, MR, NE, SN, TD, TG
     AU 9747123          A1   19980515      AU 1997-47123    19971017
     AU 737801           B2   20010830
     GB 2331522          A1   19990526      GB 1999-3117     19971017
     GB 2331522          B2   20010523
     EP 939827           A1   19990908      EP 1997-909437   19971017
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO
     CN 1234075          A    19991103      CN 1997-198883   19971017
     EP 1041152          A1   20001004      EP 2000-202432   19971017
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SK

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI

JP	2001502903	T2	20010306	JP 1998-519087	19971017
US	6235522	B1	20010522	US 1999-284011	19990405
NO	9901742	A	19990413	NO 1999-1742	19990413
KR	2000049250	A	20000725	KR 1999-703355	19990416

(FILE 'HOME' ENTERED AT 12:49:22 ON 08 MAR 2002)

FILE 'MEDLINE, AGRICOLA, CANCERLIT, SCISEARCH, CAPLUS, BIOSIS, MEDICONF'
ENTERED AT 12:49:31 ON 08 MAR 2002

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L1         22379 S RETROVIR? VECTOR?
L2          1081 S L1 AND (MULV OR MLV )
L3          1082 S L1 AND (MULV OR MLV OR MOLV)
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L8          7387 S L1 AND (MULV OR MLV OR MOMLV OR MURINE OR  MOLONEY)
L9            12 S L8 AND (HIV (S) 5-LTR)
L10            5 DUP REM L9 (7 DUPLICATES REMOVED)
L11            5 SORT L10 PY
L12          659 S L8 AND HIV
L13          224 S L12 AND (U3 OR RRE OR REV OR TAT)
L14           91 DUP REM L13 (133 DUPLICATES REMOVED)
L15           46 S L14 AND PY<=1997
L16           46 SORT L15 PY
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=> d an ti so au ab pi l16 5-7 12 18 19 20 23 24 31 36 37 39 41 44 45

L16 ANSWER 5 OF 46 MEDLINE
AN 91374609 MEDLINE
TI Resistance to human immunodeficiency virus type 1 (**HIV**-1) infection in human CD4+ lymphocyte-derived cell lines conferred by using **retroviral vectors** expressing an **HIV**-1 RNA-specific ribozyme.
SO JOURNAL OF VIROLOGY, **(1991 Oct)** 65 (10) 5531-4.
Journal code: KCV; 0113724. ISSN: 0022-538X.
AU Weerasinghe M; Liem S E; Asad S; Read S E; Joshi S
AB Toward gene therapy for the treatment of human immunodeficiency virus type 1 (**HIV**-1) infections in AIDS, **Moloney murine** leukemia virus-derived **retroviral vectors** were engineered to allow constitutive and **tat**-inducible expression of an **HIV**-1 5' leader sequence-specific ribozyme (Rz1). These vectors were used to infect the human CD4+ lymphocyte-derived MT4 cell line. The stable MT4 transformants expressing an **HIV**-1 RNA-specific ribozyme, under the control of the herpes simplex virus thymidine kinase (tk) promoter, were found to be somewhat resistant to **HIV**-1 infection as virus production was delayed. In cells allowing ribozyme expression under control of the simian virus 40 or cytomegalovirus promoter, the rate of **HIV**-1 multiplication was slightly decreased, and virus production was delayed by about 14 days. The highest level of resistance to **HIV**-1 infection was observed in MT4 cells transformed with a vector containing a fusion tk-TAR (trans activation-responsive) promoter to allow ribozyme expression in a constitutive and **tat**-inducible manner; no **HIV**-1 production was observed 22 days after infection of these cells. These results indicate that **retroviral vectors** expressing **HIV**-1 RNA-specific ribozymes can be used to confer resistance to **HIV**-1 infection.

L16 ANSWER 6 OF 46 MEDLINE
AN 91303708 MEDLINE
TI Construction of a replication-competent **murine** **retrovirus vector** expressing the human immunodeficiency virus type 1 **tat** transactivator protein.
SO JOURNAL OF VIROLOGY, **(1991 Aug)** 65 (8) 4490-3.
Journal code: KCV; 0113724. ISSN: 0022-538X.
AU Dillon P J; Lenz J; Rosen C A
AB A replication-competent Akv **murine** leukemia virus-based vector encoding the human immunodeficiency virus **tat** cDNA under control

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of the simian virus 40 early promoter sequences was constructed. The simian virus 40 **tat** sequences were placed within the **U3** region of the 3' long terminal repeat. The resulting virus, derived by transfection, replicated efficiently in mouse NIH 3T3 cells and maintained the **tat** cDNA insert. It has been suggested that **Tat** function requires the presence of a human-specific cofactor, which is absent in **murine** cells. However, infection of **murine** cells with the Akv virus encoding **tat** resulted in significant transactivation of a human immunodeficiency virus long terminal repeat-driven reporter gene, indicating that human cofactors are not always required for **Tat** function. The vector system described may be useful for introduction of foreign genes in vivo and in whole animals when virus spread is required for efficient infection and levels of gene expression.

L16 ANSWER 7 OF 46 MEDLINE
AN 92410592 MEDLINE
TI Inhibition of replication of **HIV**-1 by **retroviral vectors** expressing **tat**-antisense and anti-**tat** ribozyme RNA.
SO VIROLOGY, **(1992 Sep)** 190 (1) 176-83.
Journal code: XEA; 0110674. ISSN: 0042-6822.
AU Lo K M; Biasolo M A; Dehni G; Palu G; Haseltine W A
AB A ribozyme was constructed that specifically cleaves RNA that contains the first coding exon of the **tat** gene of **HIV**-1. This anti-**tat** ribozyme was incorporated into a **Moloney murine** leukemia virus vector. A sequence containing only the 48-nucleotide antisense region of the ribozyme was also inserted into the **retroviral vector**. Human T-cell lines constitutively producing the **tat**-antisense and the anti-**tat** ribozyme RNA were created by transduction into Jurkat cells. When challenged with **HIV**-1, both the **tat**-antisense and anti-**tat** ribozyme-producing cells inhibited the replication of **HIV**-1. The antisense vector conferred a greater resistance to **HIV**-1 replication than did the anti-**tat** ribozyme vector.

L16 ANSWER 12 OF 46 MEDLINE
AN 95229770 MEDLINE
TI **Murine retroviral vector** that induces long-term expression of **HIV**-1 envelope protein.
SO JOURNAL OF VIROLOGICAL METHODS, **(1994 Dec)** 50 (1-3) 293-311.
Journal code: HQR; 8005839. ISSN: 0166-0934.
AU Fujita K; Maldarelli F; Purcell D F; Silver J
AB A **retroviral vector** was constructed that induces long-term expression of human immunodeficiency virus type 1 (**HIV**-1) **rev**, vpu and env genes. The vector contains the neo gene and a cytomegalovirus (CMV) immediate early promoter followed by **HIV**-1 sequence. When HeLa cells were infected with viral stocks derived from this vector, about 25% of the resulting G418-resistant clones expressed **HIV**-1 envelope protein (Env), easily detectable by Western blot analysis, metabolic labelling, and syncytium formation after co-cultivation with HeLa-CD4 cells. In most cases the level of Env expression was higher than in a T cell line (H9) chronically infected with **HIV**-1. Env-expressing HeLa cell lines also expressed **Rev**, detected by transfection with a **Rev**-dependent CAT gene construct, and Vpu, detected by immunoprecipitation with a Vpu-specific antiserum. The 75% of G418-resistant HeLa cell lines that did not express Env were found to contain proviruses that had undergone deletion of env sequences corresponding to a known intron; presumably these cell lines arose as a result of infection with virions derived from spliced RNAs. This vector should be useful for studying non-transient effects of **HIV** Env, **Rev** and Vpu in tissue culture, and for the production of Env- and/or **Rev**-expressing cell lines.

L16 ANSWER 18 OF 46 MEDLINE
AN 94339688 MEDLINE
TI Inhibition of **HIV**-1 multiplication in a human CD4+ lymphocytic cell line expressing antisense and sense RNA molecules containing **HIV**-1 packaging signal and **Rev** response element(s).
SO ANTISENSE RESEARCH AND DEVELOPMENT, **(1994 Spring)** 4 (1) 19-26. Journal code: BI7; 9110698. ISSN: 1050-5261.
AU Cohli H; Fan B; Joshi R L; Ramezani A; Li X; Joshi S
AB **Moloney murine** leukemia virua (MoMuLV)-derived **retroviral vectors** were engineered to express human immunodeficiency virus type 1 (**HIV**-1) packaging (psi) signal and **Rev** response element (**RRE**) sequences in either sense or antisense orientation. The **RRE** sequences were expressed under the control of the herpes simplex virus (HSV) thymidine kinase (tk) promoter fused to the **HIV**-1 trans-activation-responsive (TAR) element, while the psi signal sequences were expressed under control of the HSV tk promoter. Both **RRE** and psi signal sequences were expressed as part of the 3' untranslated region of the neomycin phosphotransferase (neo) mRNA. The constructs were used to transfect/infect packaging cell lines and the **retroviral vector** particles released were used to infect a human CD4+ lymphocyte-derived MT4 cell line. The stable MT4 transformants, harboring proviral vector DNA expressing one to two copies of **HIV**-1 **RRE** and psi signal in either antisense or sense orientation, were each tested for their susceptibility to **HIV**-1 infection. Compared to the results obtained with the control cells lacking any of the test DNA sequences, the rate of **HIV**-1 production remained unaltered in RRE1+ (sense RNA containing a single copy of **RRE**) RNA-containing cells, whereas it was delayed in cells expressing both RRE2+ (sense RNA containing two copies of **RRE**) and RRE1- (antisense RNA containing a single copy of **RRE**) RNA-expressing cells. In cells expressing **HIV**-1 psi signal, **HIV**-1 production remained unaltered in psi + RNA-expressing cells, whereas it was delayed by up to 30 days in psi - RNA-expressing cells.(ABSTRACT TRUNCATED AT 250 WORDS)

L16 ANSWER 19 OF 46 MEDLINE
AN 94235373 MEDLINE
TI **Retrovirus vector**-mediated transfer of functional **HIV**-1 regulatory genes.
SO AIDS RESEARCH AND HUMAN RETROVIRUSES, **(1994 Jan)** 10 (1) 47-52. Journal code: ART; 8709376. ISSN: 0889-2229.
AU Garcia J V; Miller A D
AB Replication of the human immunodeficiency virus depends on the expression of its regulatory genes. We have constructed three plasmids, based on the **retrovirus vector** LXSN, that contain the **tat**, **rev**, and env (pLTRESN), the **rev** and env (pLRESN), and the nef (pLnefSN) genes of **HIV**-1. In a two-step virus rescue protocol, during which introns are removed from the DNA fragments inserted into pLXSN, these plasmids were used to establish amphotropic **retrovirus vector** producer lines for the transfer of **tat** (LtatSN), **rev** (LrevSN), and nef (LnefSN). These vectors have titers greater or equal to 10(6) CFU/ml and efficiently transduced each of these genes into a variety of human and **murine** cell lines. Representative populations of cells constitutively expressing the **tat** and **rev** genes were obtained. Cell lines transduced with LtatSN were able to trans-activate an **HIV**-LTRCAT construct, indicating the presence of a functional **Tat** protein. Similarly, cells transduced with LrevSN were able to rescue a **rev** - **HIV**-1 provirus, indicating the presence of a functional **Rev**. We also used LnefSN to obtain clones of cells expressing Nef. Our results indicate that these **retrovirus vectors** are useful reagents for the efficient transfer of functional **Tat**, **Rev**, and Nef and for the establishment of cell lines

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constitutively expressing these genes.

L16 ANSWER 20 OF 46 CAPLUS COPYRIGHT 2002 ACS
AN 1994:400882 CAPLUS
DN 121:882
TI Compositions and method for inhibition of **HIV** production
SO U.S., 20 pp. Cont.-in-part of U.S. Ser. No. 88,086, abandoned.
CODEN: USXXAM
IN Harrison, Gail; Maxwell, Ian H.; Maxwell, Francoise; Glode, L. Michael
AB A method for the selective killing of **HIV**-infected cells, via **HIV**-regulated expression of a toxin gene, is provided. Specifically, the expression of the diphtheria toxin fragment A gene is subject to tight control by cis-acting **HIV** regulatory sequences and transacting regulatory factors. Stable transformation of target cells (those cells which can be infected with **HIV**) with an **HIV** -regulated toxin gene may provide a method of protecting a host from **HIV** infection. When such a stably transformed cell becomes infected with **HIV**, induction of the toxin gene would prevent the replication and spread of the virus. HeLa cells contg. a stably integrated toxin expression construct (**HIV**-1 LTR-5' diphtheria toxin A fragment gene-3' **HIV** crs and **RRE** elements) generated 50-96% less secreted p24 antigen than control cells following transfection with **HIV** provirus. **Retroviral vectors** based on the LNSX vector (Miller and Rosman, 1989, Biotechniques) and contg. the above expression construct were prepd.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI US 5306631	A	19940426	US 1991-685601	19910415	<--
US 5554528	A	19960910	US 1993-147829	19931104	<--

L16 ANSWER 23 OF 46 MEDLINE
AN 96129243 MEDLINE
TI Genetic instability of a **MoMLV**-based antisense double-copy **retroviral vector** designed for **HIV**-1 gene therapy.
SO GENE THERAPY, **(1995 Nov)** 2 (9) 639-46.
Journal code: CCE; 9421525. ISSN: 0969-7128.
AU Junker U; Bohnlein E; Veres G
AB We constructed a **retroviral vector** encoding a mutant tRNA(imet) gene followed by a **HIV**-1 **rev**-specific antisense sequence in the **U3** region of the 3' long terminal repeat (LTR). This **Moloney murine** leukemia virus (**MoMLV**)-based double-copy **retroviral vector** was used to transduce human lymphoblastoid T-cell lines (CEM, Jurkat). In some clonal cell lines the expected short transcript initiated either from the 5' or 3' LTR tRNA-alpha **rev** gene was not detectable by Northern blot analyses of transduced, G418-resistant cells with an alpha **rev**-specific oligonucleotide probe. In other clonal cells, neither the short polymerase III transcript nor the full-length genomic polymerase II transcript (containing the 3' LTR tRNA-alpha **rev** gene) was detectable when compared with the transduced cell pool. Southern blot and DNA-polymerase chain reaction (PCR) analyses specific for the tRNA-alpha **rev** cassette in the 5' or 3' LTR of the **retroviral vector** suggested that the transfer of the 3' LTR **U3** region to the 5' LTR was incorrect in most proviruses. These data were confirmed by DNA sequence analyses of several clonal lines demonstrating deletions and insertions. In summary, our results indicate that this **retroviral vector** design with direct repeats flanking the polymerase III transcription unit plus the alpha **rev** insert is prone to genetic rearrangements and consequently not useful for the development of gene therapy protocols.

L16 ANSWER 24 OF 46 MEDLINE
AN 96002190 MEDLINE

TI **Retroviral vector** with a CMV-IE/**HIV**-TAR hybrid LTR gives high basal expression levels and is up-regulated by **HIV**-1 **Tat**.

SO GENE THERAPY, **(1995 Jun)** 2 (4) 269-78.
Journal code: CCE; 9421525. ISSN: 0969-7128.

AU Robinson D; Elliott J F; Chang L J

AB We have constructed a new **retroviral vector** by making modifications to the commonly used **Moloney murine** leukemia virus (**MoMLV**) based vector in the long terminal repeat (LTR). The changes include replacement of a portion of the **U3** region of the **MoMLV** LTR with a hybrid regulatory element consisting of the human cytomegalovirus immediate-early enhancer/promoter (CMV-IE) together with the human immunodeficiency virus transactivation response element (**HIV**-TAR). Transfection of chloramphenicol acetyl transferase (CAT) reporter constructs into a variety of human cell lines showed that the hybrid LTR with the CMV-IE/**HIV**-TAR enhancer/promoter exhibited basal expression levels which were 10- to 50-fold higher than those obtained from the wild-type **MoMLV**-LTR enhancer/promoter. Expression from the recombinant LTR was further increased in the presence of the **HIV**-**Tat** protein, and surprisingly, **Tat** up-regulated transcription from both the **HIV** and the **MoMLV** TATA boxes. In contrast, a **MoMLV** enhancer/promoter containing only the **HIV**-TAR element in the LTR did not respond to **Tat**. When stably transfected into an amphotropic packaging cell line, the modified **retroviral vector** containing the hybrid LTR plus an extended packaging signal consistently gave higher titres of retrovirus than did the parental **MoMLV** based vector. Higher basal expression levels which can be further upregulated by **Tat**, together with more efficient virion production, suggests that the modified vector should be superior for anti-**HIV** gene therapy applications as well as for other more general applications in human gene therapy.

L16 ANSWER 31 OF 46 MEDLINE

AN 97048119 MEDLINE

TI **Murine** leukemia virus-based **Tat**-inducible long terminal repeat replacement vectors: a new system for anti-human immunodeficiency virus gene therapy.

SO JOURNAL OF VIROLOGY, **(1996 Nov)** 70 (11) 8234-40.
Journal code: KCV; 0113724. ISSN: 0022-538X.

AU Cannon P M; Kim N; Kingsman S M; Kingsman A J

AB We have constructed new **murine** leukemia virus (**MLV**)-based vectors (TIN vectors) which, following integration, contain human immunodeficiency virus (**HIV**) type 1 **U3** and R sequences in place of the **MLV U3** and R regions. This provides, for the first time, single transcriptional unit **retroviral vectors** under the control of **Tat**. TIN vectors have several advantages for anti-**HIV** gene therapy applications.

L16 ANSWER 36 OF 46 CAPLUS COPYRIGHT 2002 ACS

AN 1997:308319 CAPLUS

DN 126:326062

TI **Retrovirus vectors** in gene therapy: targeting to specific cells

SO NATO ASI Ser., Ser. A (**1996**), 290(Targeting Drugs 5), 45-51
CODEN: NALSDJ; ISSN: 0258-1213

AU Kingsman, A. J.; Bae, Y.; Griffiths, J. C.; Kim, N.; Ramsdale, E. E.; Romano, G.; Soneoka, Y.; Cannon, P. M.; Kingsman, S. M.

AB A review and discussion with 34 refs. on the design of **murine** leukemia virus (**MLV**)-based vector systems that can achieve cell-specific gene expression under the control of tissue-specific regulatory signals. Delivery of **retrovirus vectors** to specific cells and design of **retrovirus vectors** with non-**MLV** cell-specific regulatory sequences are discussed. One

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example of the use of a specific regulatory sequences in a **MLV** -based vector is the authors' use of the **HIV** virus LTR to produce vectors that would express genes only in the presence of the **HIV** transactivator **Tat**.

L16 ANSWER 37 OF 46 CAPLUS COPYRIGHT 2002 ACS
AN 1997:56256 CAPLUS
DN 126:71205
TI **Retroviral vectors** for gene therapy with the therapeutic gene under control of a promoter induced by a superinfecting virus
SO PCT Int. Appl., 41 pp.
CODEN: PIXXD2
IN Kingsman, Alan John; Kingsman, Susan Mary; Cannon, Paula Marie
AB Retroviral useful in gene therapy have a regulated promoter inducible by a regulatory factor e.g. the **HIV** transactivator protein **Tat**, and at least one selected gene under its transcriptional control. In the provirus, the regulated promoter is present in the 5' long terminal repeat (LTR) in place of the 5'-LTR promoter function of the retrovirus, and the selected gene is located between the LTRs. Thus when inserted into a host cell the gene will be expressed only when the DNA provirus is exposed to the regulatory factor. Constructs using an internal ribosome entry site (IRES) to allow expression of a pair of genes from the promoter are also described. The method is demonstrated by constructing a vector carrying a lacZ gene under control of an **HIV** -1-inducible promoter.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI WO 9637623	A1	19961128	WO 1996-GB1230	19960522	<--
W: JP, US					
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
EP 827545	A2	19980311	EP 1996-914342	19960522	
EP 827545	B1	20020227			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE, FI					
JP 11511005	T2	19990928	JP 1996-535494	19960522	
EP 1164196	A1	20011219	EP 2001-119879	19960522	
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE, FI					
US 6096538	A	20000801	US 1997-952948	19971119	

L16 ANSWER 39 OF 46 CAPLUS COPYRIGHT 2002 ACS
AN 1996:428590 CAPLUS
DN 125:78548
TI Modified **retroviral vectors** containing hybrid long terminal repeat, cytomegalovirus-IE/**HIV**-1-TAR/**Moloney murine** leukemia virus LTR, and vector use for high-level product production by recombinant technology
SO PCT Int. Appl., 125 pp.
CODEN: PIXXD2
IN Chang, Lung-Ji
AB Novel **retroviral vectors** were constructed by modifying the **Moloney murine** leukemia virus (**MoMLV**) long terminal repeat (LTR). A portion of the **U3** region of the **MoMLV** LTR was replaced with the human cytomegalovirus immediate-early enhancer/promoter (CMV-IE) together with the human immunodeficiency virus type 1 (**HIV**-1) transactivation response element (TAR). Transfection studies involving the hybrid CMV-IE/ **HIV**-1-TAR **MoMLV** LTR enhancer/promoter demonstrated that this regulatory element increases basal transcriptional levels 10- to 50-fold. Expression from the recombinant **MoMLV** LTR was further increased by the addn. of **HIV**-1 **Tat**. Addnl. vector modifications included the addn. of an **HIV**-1 extended packaging signal and 3' splice acceptor site. Modified **retroviral vectors** contg. the hybrid LTP should be useful for the prodn. of high levels of retroviral and cellular expression products.

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	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9614332	A1	19960517	WO 1995-US14576	19951108 <--
	W: AU, BR, CA, JP, KR, MX, SG, US				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	US 5693508	A	19971202	US 1994-336132	19941108 <--
	AU 9643215	A1	19960531	AU 1996-43215	19951108 <--
	AU 710180	B2	19990916		
	EP 791010	A1	19970827	EP 1995-942848	19951108 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	JP 10509318	T2	19980914	JP 1995-515515	19951108

L16 ANSWER 41 OF 46 MEDLINE
AN 97358644 MEDLINE
TI Evaluation of PCR and ELISA assays for screening clinical trial subjects for replication-competent retrovirus.
SO HUMAN GENE THERAPY, **(1997 Jul 1)** 8 (10) 1231-41.
Journal code: A12; 9008950. ISSN: 1043-0342.
AU Martineau D; Klump W M; McCormack J E; DePolo N J; Kamantigue E; Petrowski M; Hanlon J; Jolly D J; Mento S J; Sajjadi N
AB Gene delivery via **murine**-based recombinant **retroviral vectors** is currently widely used in gene therapy clinical trials. The vectors are engineered to be replication defective by replacing the structural and nonstructural genes of a cloned infectious retrovirus with a therapeutic gene of interest. The retroviral particles are currently generated in packaging cell lines, which supply all retroviral proteins in trans. Recombination between short homologous regions of the **retroviral vector** and packaging cell line elements can theoretically generate replication-competent retrovirus (RCR) and hence the Food and Drug Administration (FDA) requires the monitoring of clinical trial subjects for the presence of RCR. Sensitive polymerase chain reaction (PCR) assays have been used for the detection of **murine** leukemia virus (**MLV**) nucleotide sequences in peripheral blood mononuclear cells (PBMCs). A novel serological enzyme-linked immunosorbent assay (ELISA) for the detection of anti-**MLV** specific immunoglobulin (Ig) has been developed to be used as an alternative to the PCR assay. Both assays were used to monitor human immunodeficiency virus (**HIV**)-positive clinical trial subjects who had received multiple injections of **HIV**-IT (V), a **retroviral vector** encoding **HIV**-1 IIIBenv/**rev**. Western blot analysis and an in vitro vector neutralization assay were used to characterize further a subset of serum samples tested by ELISA. Results show no evidence of RCR infection in clinical trial subjects. PCR and ELISA assays are discussed in terms of their advantages and limitations as routine screening assays for RCR. The PCR assay is our current choice for monitoring clinical trial subjects receiving direct administration of vector, and the ELISA is our choice for those receiving ex vivo treatment regimens.

L16 ANSWER 44 OF 46 CAPLUS COPYRIGHT 2002 ACS
AN 1998:17967 CAPLUS
DN 128:57453
TI Anti-**HIV** ribozymes designed to cleave the **tat** gene or **tat/rev** common exon
SO U.S., 11 pp. Cont. of U.S. Ser. No. 355,244, abandoned.
CODEN: USXXAM
IN Rossi, John J.
AB Ribozymes targeted against two portions of the **HIV**-1 genome were designed to cleave **HIV** RNA in the **tat** gene (**TAT**) or in a common exon for **tat** and **rev** (TR). The ribozymes were cloned into the LN (LTR-neomycin) **retroviral vector** plasmids and expressed as part of vital LTR-driven transcripts. The vectors were packaged as amphotropic virions and used to transduce human T-lymphocytes. Expression of the vector transcripts

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contg. the ribozyme sequences were readily detected by Northern blot anal. of the transduced T cells. The most effective ribozyme expression was derived from the **Moloney murine** leukemia virus LTR, which resulted in long, multifunctional, viral length transcripts. The T-lymphocytes expressing the anti-**HIV**-1 ribozymes showed resistance to **HIV**-1 replication.

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	US 5695938	A	19971209	US 1996-654773	19960529	<--
	US 5985661	A	19991116	US 1997-909768	19970812	

L16 ANSWER 45 OF 46 CAPLUS COPYRIGHT 2002 ACS
AN 1997:318220 CAPLUS
DN 126:289038
TI **Retroviral vectors** and method of use for nucleic acid delivery to non-dividing cells
SO PCT Int. Appl., 34 pp.
CODEN: PIXXD2
IN Verma, Inder; Trono, Didier; Naldini, Luigi; Gallay, Philippe
AB A recombinant retrovirus capable of infecting a non-dividing cell and a method of producing such a virus is provided. The recombinant retrovirus is preferably of lentivirus origin and is useful for the treatment of a variety of disorders including neurol. disorders and disorders of other non-dividing cells. The above method differs from the std. helper virus/packaging cell line method in that (1) three or more individual vectors, which contain all of the required genes for prodn. or a recombinant virus for infection and transfer of nucleic acid to nondividing cells, are used to co-transfect a suitable packaging cell line, and (2) there is therefore no need for a helper virus. Thus, a first vector contains viral, preferably lentiviral, gag and pol genes. A second vector provides an env gene, which can be derived from any virus, operably assocd. with viral regulatory sequences, e.g. a promoter and/or enhancer. A third vector provides the cis-acting viral sequences necessary for the viral life cycle, e.g. the .phi. packaging sequence, reverse transcription signals, integration signals, viral promoter, enhancer, and polyadenylation sequences. This third vector also contains a cloning site for the heterologous nucleic acid to be transferred to a non-dividing cell. The system was demonstrated using **HIV**-based vectors. Efficiency of transduction into non-dividing cells in vitro was dependent on the stage of cell cycle arrest. Infection of G1/S and G2 arrested cells was as efficient as that obsd. with growing cells. Infection of G0 arrested cells was less efficient, but the vector survived as a stable intermediate which could be rescued by stimulation of the cells to divide.

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 9712622	A1	19970410	WO 1996-US15406	19960926	<--
	W: AU, CA, IL, JP					
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
	US 6013516	A	20000111	US 1995-540259	19951006	
	AU 9671681	A1	19970428	AU 1996-71681	19960926	<--
	AU 720993	B2	20000622			
	EP 871459	A1	19981021	EP 1996-933140	19960926	
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
	JP 11512615	T2	19991102	JP 1996-514319	19960926	
	ZA 9608382	A	19970627	ZA 1996-8382	19961004	<--

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(FILE 'HOME' ENTERED AT 12:49:22 ON 08 MAR 2002)

FILE 'MEDLINE, AGRICOLA, CANCERLIT, SCISEARCH, CAPLUS, BIOSIS, MEDICONF'
ENTERED AT 12:49:31 ON 08 MAR 2002

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L1         22379 S RETROVIR? VECTOR?
L2          1081 S L1 AND (MULV OR MLV )
L3          1082 S L1 AND (MULV OR MLV OR MOLV)
L4           189 S L1 (L) 5(W)LTR
L5            55 S L4 AND (U3 OR RRE OR REV OR TAT)
L6            21 DUP REM L5 (34 DUPLICATES REMOVED)
L7            21 SORT L6 PY
L8          7387 S L1 AND (MULV OR MLV OR MOMLV OR MURINE OR  MOLONEY)
L9            12 S L8 AND (HIV (S) 5-LTR)
L10            5 DUP REM L9 (7 DUPLICATES REMOVED)
L11            5 SORT L10 PY
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L11 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2002 ACS
AN 1998:268634 CAPLUS
DN 128:304785
TI Construction and characterization of HIV and other lentiviral vectors
SO PCT Int. Appl., 31 pp.
CODEN: PIXXD2
IN Kingsman, Alan John; Kingsman, Susan Mary
AB **Retroviral vector** particles capable of infecting and transducing non-dividing mammalian target cells, which vector particles may be based on lentiviruses such as **HIV** and which have an RNA genome constructed so as to provide in the DNA provirus a non-lentiviral expression control element in the **5'LTR** of the provirus. These vectors, designated LLD (for lentiviral LTR-deleted) can be used to infect and transduce mammalian cells. The method is exemplified by use of the U3 and promoter regions of **murine** leukemia virus in construction of LLD vectors.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9817816	A1	19980430	WO 1997-GB2858	19971017
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9747123	A1	19980515	AU 1997-47123	19971017
AU 737801	B2	20010830		
GB 2331522	A1	19990526	GB 1999-3117	19971017
GB 2331522	B2	20010523		
EP 939827	A1	19990908	EP 1997-909437	19971017
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
CN 1234075	A	19991103	CN 1997-198883	19971017
EP 1041152	A1	20001004	EP 2000-202432	19971017
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001502903	T2	20010306	JP 1998-519087	19971017
US 6235522	B1	20010522	US 1999-284011	19990405
NO 9901742	A	19990413	NO 1999-1742	19990413
KR 2000049250	A	20000725	KR 1999-703355	19990416

(FILE 'HOME' ENTERED AT 12:49:22 ON 08 MAR 2002)

FILE 'MEDLINE, AGRICOLA, CANCERLIT, SCISEARCH, CAPLUS, BIOSIS, MEDICONF' ENTERED AT 12:49:31 ON 08 MAR 2002

L1 22379 S RETROVIR? VECTOR?
L2 1081 S L1 AND (MULV OR MLV)
L3 1082 S L1 AND (MULV OR MLV OR MOLV)
L4 189 S L1 (L) 5(W)LTR
L5 55 S L4 AND (U3 OR RRE OR REV OR TAT)
L6 21 DUP REM L5 (34 DUPLICATES REMOVED)
L7 21 SORT L6 PY

=> d an ti so au ab pi l7 11 12 14 16 18

L7 ANSWER 11 OF 21 CAPLUS COPYRIGHT 2002 ACS
AN 1997:56256 CAPLUS
DN 126:71205
TI Retroviral vectors for gene therapy with the therapeutic gene under control of a promoter induced by a superinfecting virus
SO PCT Int. Appl., 41 pp.
CODEN: PIXXD2
IN Kingsman, Alan John; Kingsman, Susan Mary; Cannon, Paula Marie
AB Retroviral useful in gene therapy have a regulated promoter inducible by a regulatory factor e.g. the HIV transactivator protein **Tat**, and at least one selected gene under its transcriptional control. In the provirus, the regulated promoter is present in the 5' long terminal repeat (LTR) in place of the 5'-LTR promoter function of the retrovirus, and the selected gene is located between the LTRs. Thus when inserted into a host cell the gene will be expressed only when the DNA provirus is exposed to the regulatory factor. Constructs using an internal ribosome entry site (IRES) to allow expression of a pair of genes from the promoter are also described. The method is demonstrated by constructing a vector carrying a lacZ gene under control of an HIV-1-inducible promoter.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9637623	A1	19961128	WO 1996-GB1230	19960522
W: JP, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 827545	A2	19980311	EP 1996-914342	19960522
EP 827545	B1	20020227		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE, FI				
JP 11511005	T2	19990928	JP 1996-535494	19960522
EP 1164196	A1	20011219	EP 2001-119879	19960522
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE, FI				
US 6096538	A	20000801	US 1997-952948	19971119

L7 ANSWER 12 OF 21 MEDLINE
AN 97388537 MEDLINE
TI Co-packaging of non-vector RNAs generates replication-defective retroviral vector particles: a novel approach for blocking retrovirus replication.
SO NUCLEIC ACIDS RESEARCH, (1997 Aug 15) 25 (16) 3199-203.
Journal code: O8L; 0411011. ISSN: 0305-1048.
AU Joshi S; Ding S F; Liem S E
AB A Moloney murine leukemia virus (MoMuLV)-derived packaging **retroviral vector**, pUCMoTN-PR3, was previously developed in which the packaging (psi) signal was cloned within the 5'-long terminal repeat (LTR) **U3**-r and U5 sequences. The MoTN-PR3 vector particles released from a transfected packaging cell line contain RNAs with r-psi-U5 sequences at the 5'-end and **U3**-r sequences at the 3'-end. Upon infection, these vector particles can efficiently transduce the neomycin phosphotransferase (neo) gene to the target cells. The structure of the proviral DNA synthesized in these cells was shown to contain modified 5'- and 3'-LTRs with **U3**-r-psi-U5 sequences,

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indicating that this vector can undergo reverse transcription and integration. Analysis of psi signal-containing RNAs revealed that in addition to vector RNA transcribed from the MoMuLV **5'-LTR** promoter, readthrough neo RNA transcribed from the internal herpes simplex virus (HSV) thymidine kinase (tk) promoter and cellular RNAs transcribed from the MoMuLV 3'-LTR promoter are produced. Of these, the downstream cellular RNAs are also packaged within the vector particles. These vector particles containing the vector and non-vector RNAs carrying the MoMuLV psi signal are non-infectious. It is proposed that intracellular expression of packageable non-viral RNAs may represent an effective strategy for inhibiting animal and plant virus replication.

L7 ANSWER 14 OF 21 CAPLUS COPYRIGHT 2002 ACS
AN 1998:268634 CAPLUS
DN 128:304785
TI Construction and characterization of HIV and other lentiviral vectors
SO PCT Int. Appl., 31 pp.
CODEN: PIXXD2
IN Kingsman, Alan John; Kingsman, Susan Mary
AB **Retroviral vector** particles capable of infecting and transducing non-dividing mammalian target cells, which vector particles may be based on lentiviruses such as HIV and which have an RNA genome constructed so as to provide in the DNA provirus a non-lentiviral expression control element in the **5'LTR** of the provirus. These vectors, designated LLD (for lentiviral LTR-deleted) can be used to infect and transduce mammalian cells. The method is exemplified by use of the **U3** and promoter regions of murine leukemia virus in construction of LLD vectors.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9817816	A1	19980430	WO 1997-GB2858	19971017
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9747123	A1	19980515	AU 1997-47123	19971017
AU 737801	B2	20010830		
GB 2331522	A1	19990526	GB 1999-3117	19971017
GB 2331522	B2	20010523		
EP 939827	A1	19990908	EP 1997-909437	19971017
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
CN 1234075	A	19991103	CN 1997-198883	19971017
EP 1041152	A1	20001004	EP 2000-202432	19971017
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001502903	T2	20010306	JP 1998-519087	19971017
US 6235522	B1	20010522	US 1999-284011	19990405
NO 9901742	A	19990413	NO 1999-1742	19990413
KR 2000049250	A	20000725	KR 1999-703355	19990416

L7 ANSWER 16 OF 21 CAPLUS COPYRIGHT 2002 ACS
AN 1999:451386 CAPLUS
DN 131:83977
TI Retroviral vector for targeted gene expression and its use in gene therapy
SO PCT Int. Appl., 38 pp.
CODEN: PIXXD2
IN Gunzburg, Walter; Klein, Dieter; Tabotta, Walter; Salmons, Brian
AB The present invention relates to a **retroviral vector** which is esp. applicable as a safe gene transfer vehicle for targeted gene

therapy. Said **retroviral vector** comprises one or more promoters inserted in antisense orientation within the **5'** **LTR** region and one or more coding sequences inserted in antisense orientation within the 3'LTR region. Both the promoter and the coding sequence are addnl. inserted in such a way as to ensure that the promoter and the coding sequence become duplicated during the process of reverse transcription in a target cell and thus appear in the 3' as well as in the **5'LTR** region of the resulting provirus in a fashion where the promoter is located upstream of the coding sequence, thereby allowing it to drive gene expression. This system avoids any leakiness of gene expression in the packaging cells and allows expression of transferred genes in the target cell without the necessity for external stimuli.

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9935280	A1	19990715	WO 1999-EP2	19990103
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 9924195	A1	19990726	AU 1999-24195	19990103
	EP 1045922	A1	20001025	EP 1999-903600	19990103
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

L7 ANSWER 18 OF 21 CAPLUS COPYRIGHT 2002 ACS
AN 2000:15396 CAPLUS
DN 132:74529
TI High efficiency retroviral vectors that contain none of viral coding sequences
SO PCT Int. Appl., 70 pp.
CODEN: PIXXD2
IN Kim, Sunyoung; Yu, Seung Shin; Kim, Jong-mook
AB The present invention relates to improved **retroviral vectors** for gene therapy. In this invention, **retroviral vectors** with higher safety and efficiency are constructed from murine leukemia virus (MLV)-based starting vectors, MON and MIN. The improved vectors have following features: (1) sequences corresponding to MLV-derived pol gene are completely deleted in the vectors, avoiding homologous recombination which has been a baffling problem in conventional **retroviral vectors**; (2) a heterologous intron, splicing acceptor and/or non-coding sequence are/is inserted into the upstream position of cloning site, maximizing the expression of a foreign gene through efficient splicing; (3) the vectors contain either the full-length **U3** sequence of **5'** **LTR** or a strong heterologous promoter instead, permitting the abundant prodn. of RNA; (4) either IRES (internal ribosomal entry site) or internal SV40 minimal promoter is inserted into the downstream position of cloning site, enabling the simultaneous expression of two or more foreign genes. Thus, the MLV-based DONSA1 vector is constructed wherein the splicing acceptor of mouse Ig gene and exon 1 of human cytomegalovirus ie1 (UL123) gene are inserted into the upstream position of the cloning site for the foreign gene; the full-length **U3** sequence (-419 to -1 bp) of MLV **5'** **LTR** is replaced with HCMV major immediate-early promoter, and SV40 minimal promoter is inserted into the downstream position of cloning site for the foreign gene. Since the improved **retroviral vectors** of this invention turn out to be safe and to express the foreign gene efficiently, they are useful for gene therapy and the like.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

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PI	WO 2000000629	A1	20000106	WO 1999-KR334	19990624
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	KR 2000006334	A	20000125	KR 1999-23398	19990622
	AU 9946554	A1	20000117	AU 1999-46554	19990624
	EP 1032697	A1	20000906	EP 1999-929919	19990624
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

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